Secretory Functions of the Alimentary Tract

General Principles of Alimentary Tract Secretion

Anatomical Types of Glands

Single-cell mucous glands / goblet Cells : On the surface of the epithelium in most parts of the GI tract are, *mucus secretion mainly in response to local irritation* of the epithelium.

*Crypts of Lieberkühn: m*any surface areas of the GI tract are lined by *pits that represent* invaginations of the epithelium into the submucosa, In the small intestine, these pits, *are deep and contain specialized secretory* cells.

Tubular gland: In the stomach and upper duodenum are large numbers of deep *tubular glands. Eg. acid- and* pepsinogen-secreting gland of the stomach (oxyntic gland).

Complex glands: *salivary glands, pancreas, and liver—that provide secretions for digestion or emulsification* of food. The salivary glands and the pancreas are compound acinous glands, lying outside the walls of the GI tract , contain millions of *acini lined with secreting glandular cells; these acini feed into a system of ducts that* finally empty into the alimentary tract itself.

Basic Mechanisms of Stimulation of the Alimentary Tract Glands

➢Direct contact stimulation of the **surface glandular cells** by the food.

➢Local epithelial stimulation also activates the ***enteric nervous system*** *of the gut wall.*
(1) tactile stimulation,
(2) chemical irritation,
(3) distention of the gut wall.
The resulting nervous reflexes stimulate both the mucous cells on the gut epithelial surface and the deep glands in the gut wall to increase their secretion.

➢**Autonomic Stimulation of Secretion**

(1) Parasympathetic Stimulation: Increase secretion in glands in the upper portion of the tract (innervated by the glossopharyngeal and vagus parasympathetic nerves) such as the salivary, esophageal, gastric glands, pancreas, and Brunner's glands in the duodenum. glands in the distal portion of the large intestine, innervated by pelvic parasympathetic nerves.
(2) Sympathetic Stimulation: dual effect, stimulation alone usually slightly increases secretion. If parasympathetic or hormonal stimulation is already causing copious secretion by the glands, superimposed sympathetic stimulation usually reduces the secretion, because of vasoconstrictive reduction of the blood supply.

➢**Regulation of Glandular Secretion by Hormones.** polypeptides

Basic Mechanism of Secretion by Glandular Cells

Secretion of Organic Substances.

1. Nutrient material needed for formation of the secretion must first diffuse or be actively transported by the blood in the capillaries into the base of the glandular cell.

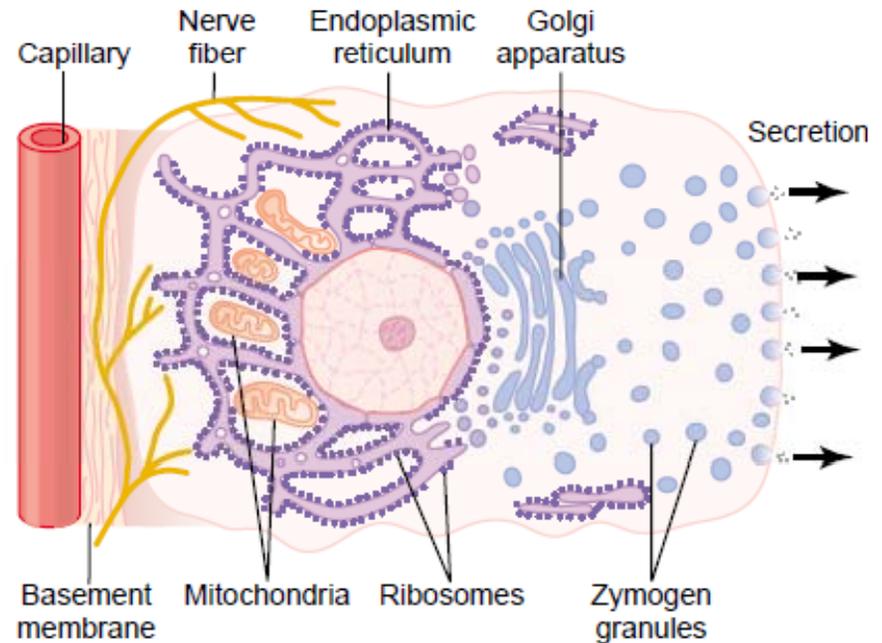2. Many *mitochondria located inside the glandular* cell near its base use oxidative energy to form ATP.

Figure 64–1

Typical function of a glandular cell for formation and secretion of enzymes and other secretory substances.

3. Energy from the ATP, along with appropriate substrates provided by the nutrients, is then used to synthesize the organic secretory substances; almost entirely in the ER *and Golgi complex. Ribosomes adherent to the* reticulum are specifically responsible for formation of the proteins that are secreted

4. The secretory materials are transported through the tubules of the ER, passing in about 20 min all the way to the vesicles of the Golgi complex.

5. In the Golgi complex, the materials are modified, added to, concentrated, and discharged into the cytoplasm in the form of *secretory vesicles, which* are stored in the apical ends of the secretory cells.
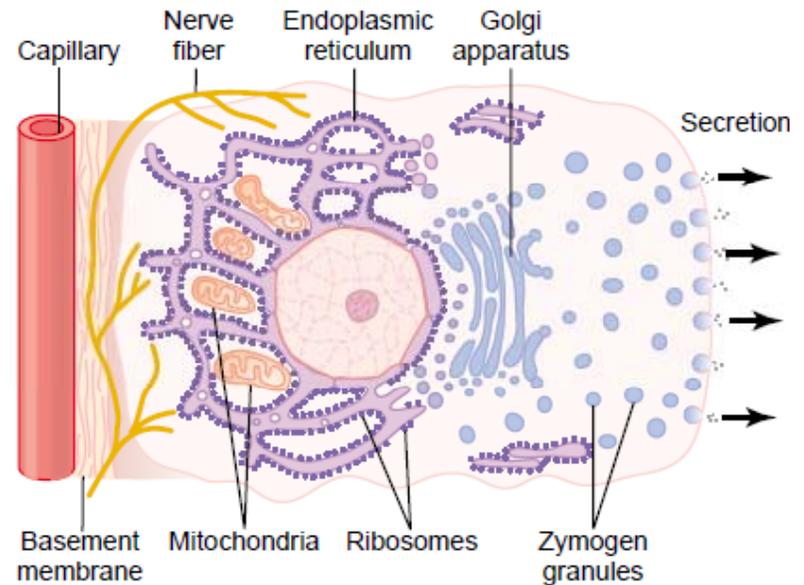
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Figure 64–1

Typical function of a glandular cell for formation and secretion of enzymes and other secretory substances.
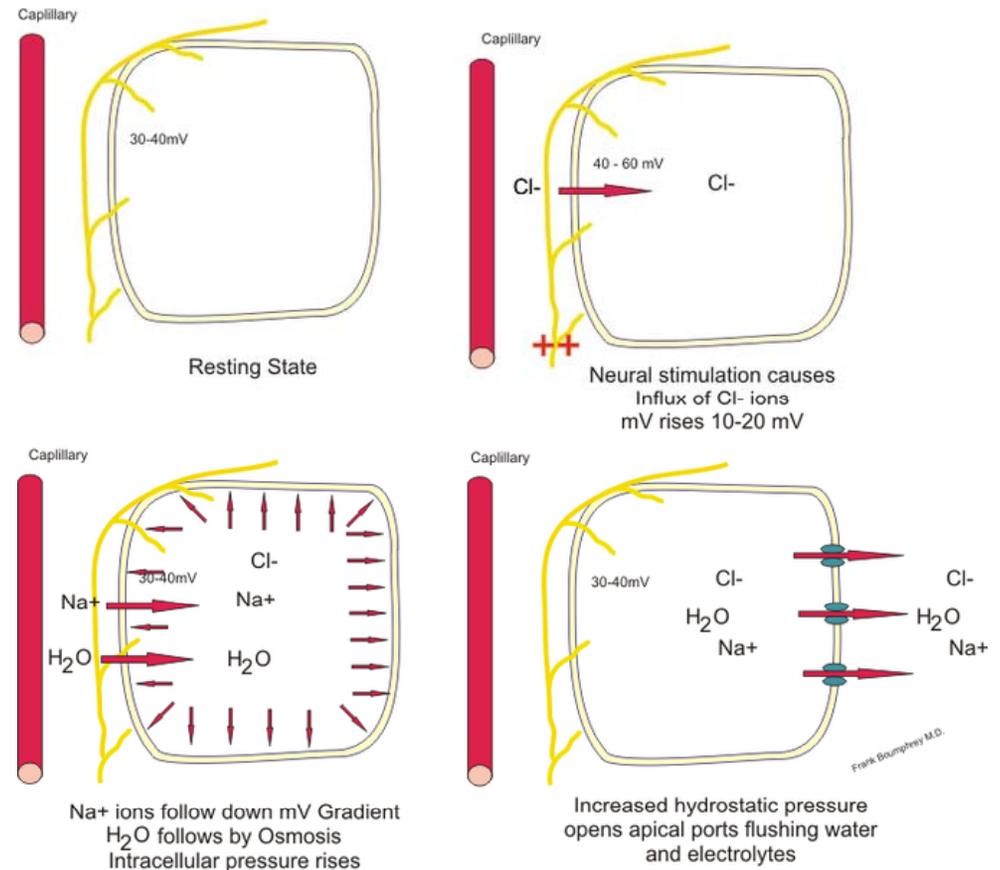
6. These vesicles remain stored until nervous or hormonal control signals cause the cells to extrude the vesicular contents through the cells' surface, in the following way:
   a. The control signal first *increases the cell membrane permeability to calcium ions, and* calcium enters the cell.
   b. The *calcium in turn causes* many of the vesicles to fuse with the apical cell membrane.
   c. The apical cell membrane breaks open, thus emptying the vesicles to the exterior; this process is called *exocytosis*

Water and Electrolyte Secretion.

A second necessity for glandular secretion is secretion of sufficient water and electrolytes to go along with the organic substances.

1. Nerve stimulation of the *basal portion of the cell membrane causes active* transport of Cl- ions to the cell interior.

2. Resulting increase in electronegativity inside the cell causes +ive ions such as *Na+ ions to move inside* the cell.

3. Excess of both -ive and +ive ions inside the cell creates an osmotic force that causes osmosis of water increasing the hydrostatic pressure inside   the cell.

Caplillary

30-40mV

Resting State

Caplillary

40 - 60 mV

Cl-   Cl-

++

Neural stimulation causes
Influx of Cl- ions
mV rises 10-20 mV

Caplillary

Cl-
30-40mV
Na+   Na+

H₂O   H₂O

Na+ ions follow down mV Gradient
H₂O follows by Osmosis
Intracellular pressure rises

Caplillary

30-40mV   Cl-   Cl-
              H₂O   H₂O
              Na+   Na+

Frank Brumphrey M.D.

Increased hydrostatic pressure
opens apical ports flushing water
and electrolytes

4. The pressure opens minute openings of the secretory border of the cell, causing flushing of water, electrolytes, and organic materials out of the secretory end of the glandular cell.

Lubricating and Protective Properties of Mucus, and Importance of Mucus in the GI Tract

Mucus is a thick secretion composed mainly of water, electrolytes, and a mixture of several glycoproteins .

Mucus is slightly different in different parts of the GI tract , everywhere it has several important characteristics that make it both an excellent lubricant and a protectant for the wall of the gut.

a. Adherent qualities that make it adhere tightly to the food or other particles and to spread as a thin film over the surfaces.
b. *Sufficient body that* it coats the wall of the gut and prevents actual contactof most food particles with the mucosa.
c. *L*ow resistance for slippage, so that the particles can slide along the epithelium with great ease.
d. Causes fecal particles to adhere to one another to form the feces that are expelled during a bowel movement.
e. *Strongly resistant to digestion by* the GI enzymes.
f. T*he glycoproteins* of mucus have amphoteric properties, which means that they are capable of buffering small amounts of either acids or alkalies; also, mucus often contains moderate quantities of bicarbonate ions which specifically neutralize acids.

Secretion of Saliva

Salivary Glands; Characteristics of Saliva.

The principal glands of salivation are the **parotid,
submandibular,** and **sublingual glands**; *in addition,
there are many very* small **buccal glands**. *Daily
secretion of saliva normally* ranges between 800 and
1500 ml.

Buccal gland

Sublingual gland

Parotid gland

Submandibular gland
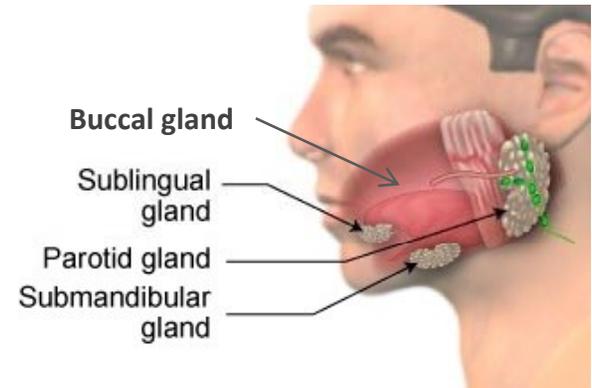
Saliva contains two major types of protein secretion:

(1) serous secretion *that contains ptyalin (an* a-amylase), an enzyme for digesting
    starches.
(2) mucus secretion *that contains mucin for lubricating* and for surface protective
    purposes.

Parotid glands secrete serous.
Buccal glands secrete mucus.
Submandibular and sublingual glands secrete both serous and mucus.

Saliva has a pH between 6.0 and 7.0, favorable range for the digestive action of
ptyalin.

Table 64-1 Daily Secretion of Intestinal Juices

	Daily Volume (ml)	pH
Saliva	1000	6.0-7.0
Gastric secretion	1500	1.0-3.5
Pancreatic secretion	1000	8.0-8.3
Bile	1000	7.8
Small intestine secretion	1800	7.5-8.0
Brunner's gland secretion	200	8.0-8.9
Large intestinal secretion	200	7.5-8.0
Total	6700	

Secretion of Ions in Saliva

Saliva contains large quantities of K+ & HCO3- ions. Conc of both Na+ and Cl- ions are several times less in saliva than in plasma.

Salivary secretion is a two-stage operation:

1. The acini secrete a *primary secretion* that contains ptyalin and/or mucin in a solution of ions in conc similar to ECF.
2. As the primary secretion flows through the ducts, two major active transport processes:

(i) *Na+ ions* are actively reabsorbed from all the salivary ducts and *K+ ions* are actively secreted in exchange for the Na+, creating electrical negativity of about −70 mV in the salivary ducts; this in turn causes Cl- ions to be reabsorbed passively.

(ii) *HCO3- ions* are secreted by the ductal epithelium into the lumen of the duct, partly by passive exchange of HCO3- for Cl- ions, partly from an active secretory process.
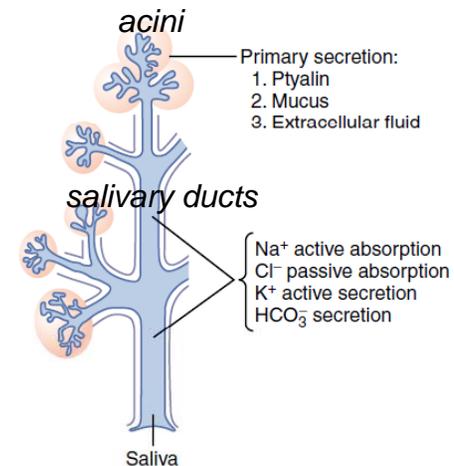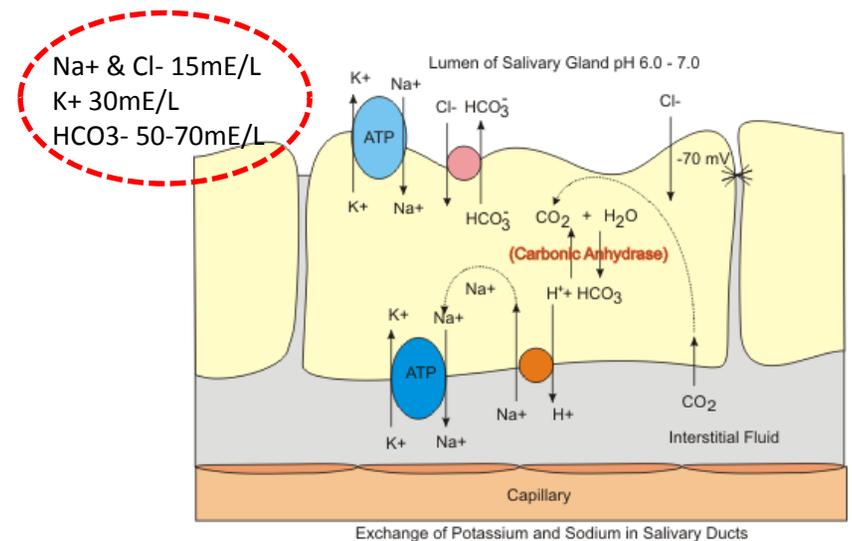

Figure 64-2 Formation and secretion of saliva by a submandibular salivary gland.

Na+ & Cl- 15mE/L
K+ 30mE/L
HCO3- 50-70mE/L

Lumen of Salivary Gland pH 6.0 - 7.0

Exchange of Potassium and Sodium in Salivary Ducts

Frank Boumphrey M.D. 2009

Function of Saliva for Oral Hygiene

Under basal awake conditions, about 0.5 ml of saliva, almost entirely of the mucous type, is secreted each minute; but during sleep, little secretion occurs.

Saliva helps prevent the deteriorative processes in the mouth by several ways.

1. Flow of saliva itself helps wash away pathogenic bacteria, as well as food particles that provide their metabolic support.

2. Contains several factors that destroy bacteria, *thiocyanate ions, proteolytic enzymes*—most important, *lysozyme*—that (a) attack the bacteria, (b) aid the thiocyanate ions in entering the bacteria where these ions in turn become bactericidal, and (c) digest food particles, thus helping further to remove the bacterial metabolic support.

3. Often contains significant amounts of antibodies that can destroy oral bacteria, including some that cause dental caries.

 In the absence of salivation, oral tissues often become ulcerated and otherwise infected, and caries of the teeth can become rampant.

Nervous Regulation of Salivary Secretion

➢Controlled mainly by **parasympathetic nervous signals** all the way from the superior and inferior salivatory nuclei in the brain stem.

➢Excited by both taste and tactile stimuli from the tongue and other areas of the mouth and pharynx.

➢Can be stimulated or inhibited by nervous signals arriving in the salivatory nuclei from higher centers of the CNS (appetite center).

➢In response to **reflexes originating in the stomach and upper small intestines** (irritant), nausea due to GI abnormality., to dilute or neutralizie the irritant.

Figure 64-3 Parasympathetic nervous regulation of salivary secretion.

➢**Sympathetic stimulation** to a lesser extent through cervical nerves from superior cervical ganglia .

➢**Vasodilation** by either PNS or by kallikrein secreted by the activated salivary cells, which splits alpha2-globulin in the blood to form bradykinin, a strong vasodilator.
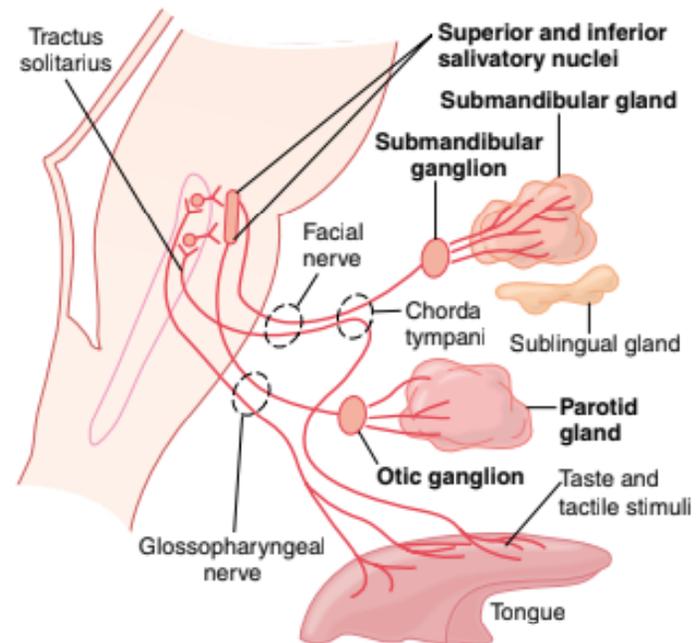
Esophageal secretions

➢ Entirely mucous and mainly provide lubrication for swallowing.

➢ Esophagus is lined with many **simple mucous glands.**

➢ At the gastric end and to a lesser extent in the initial portion of the esophagus, there are also many **compound mucous glands.**

➢ Compound glands in the upper esophagus prevents mucosal excoriation by newly entering food.

➢ Compound glands located near the esophagogastric junction protect the esophageal wall from digestion by acidic gastric juices that often reflux from the stomach back into the lower esophagus.

➢ Despite this protection, a peptic ulcer at times can still occur at the gastric end of the esophagus.

Gastric Secretion

Characteristics of the Gastric Secretions

➢In addition to **mucus-secreting cells** that line the entire surface of the stomach, the stomach mucosa has two important types of tubular glands: **oxyntic glands (also called gastric glands)** and **pyloric glands.**

➢The oxyntic (acid-forming) glands secrete HCl, pepsinogen, intrinsic factor, and mucus, located in the body & fundus (80%) of stomach.

➢The pyloric glands secrete mainly mucus for protection of the pyloric mucosa from the stomach acid. They also secrete the hormone gastrin, located in the antral portion of the stomach (20 % of the stomach).

# Secretions from the Oxyntic (Gastric) Glands

Composed of 3 types of cells: (1) mucous neck cells, secrete mainly mucus; (2) peptic (or chief) cells, secrete large quantities of pepsinogen; and (3) parietal (or oxyntic) cells, secrete HCl & intrinsic factor.

Secretion of HCl by the parietal cells involves special mechanisms:
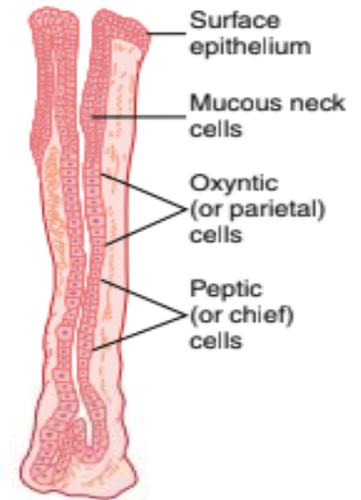
➢When stimulated, the parietal cells secrete an acid solution that contains about 160 mmol/L of HCl nearly, pH 0.8.

➢Hydrogen ion conc is 3 million times that of the arterial blood. To concentrate the hydrogen ions more than 1500 calories of energy per liter of gastric juice is required.
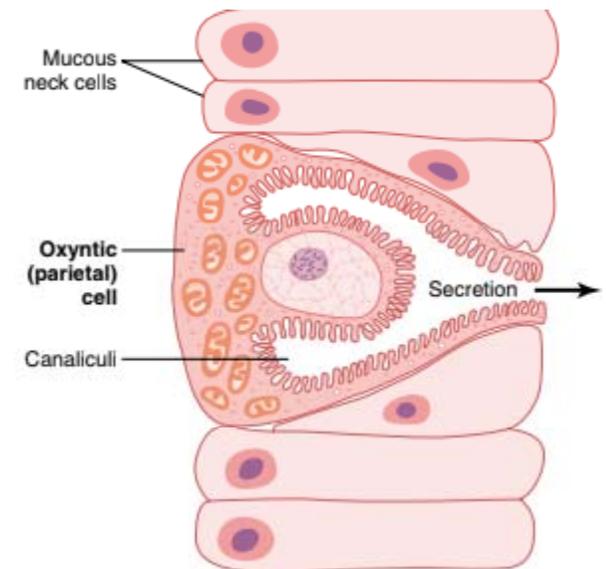
➢Parietal cell contains large branching intracellular canaliculi. The HCl formed at the villus-like projections inside these canaliculi and is then conducted through the canaliculi to the secretory end of the cell.

Chemical mechanism of HCl formation

1. Water inside the parietal cell dissociates into H+ and OH− . The H+ is actively secreted into the canaliculus in exchange for K+, by H+- K+ ATPase.

2. K+ ions transported into the cell by the Na+-K+ ATPase pump on the basolateral side of the membrane tend to leak into the lumen but are recycled back into the cell by the H+-K+ ATPase.

3. The basolateral Na+-K+ ATPase creates low intracellular Na+, which contributes to Na+ reabsorption from the lumen of the canaliculus.
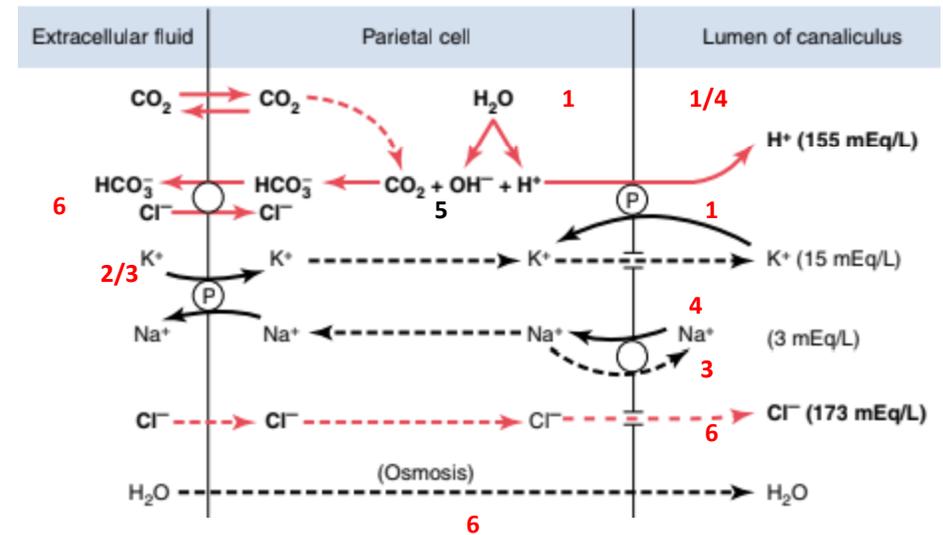
4. Thus, most of the K+ and Na+ in the canaliculus is reabsorbed into the cell cytoplasm, and H+ ions take their place in the canaliculus.

5. The pumping of H+ out of the cell by the H+-K+ ATPase permits OH− to accumulate and form HCO3 − from CO2 (metabolic product/enter from blood),carbonic anhydrase)

6. The HCO3 − is then transported to the ECF in exchange for Cl- ions, which enter the cell and are secreted through Cl- channels into the canaliculus, forming HCl, which is secreted into the lumen. Water passes into the lumen by osmosis because of extra ions in the canaliculus.

Prevention of back leak of acid

➤A major part of the stomach's ability to prevent back leak of acid can be attributed to the gastric barrier due to the formation of **alkaline mucus (surface mucosal cells)** and to **tight junctions** between epithelia cells.

➤If this barrier is damaged by toxic substances, such as occurs with excessive use of aspirin or alcohol, the secreted acid does leak down an electrochemical gradient into the mucosa, causing stomach mucosal damage.

Basic Factors That Stimulate Gastric Secretion
(Acetylcholine, Gastrin, and Histamine)
.
➤Acetylcholine released by parasympathetic stimulation excites secretion of pepsinogen by peptic cells, HCl by parietal cells, and mucus by mucous cells.

➤Both gastrin and histamine strongly stimulate secretion of acid by parietal cells but have little effect on the other cells.

Secretion of Intrinsic Factor by Parietal Cells.

Intrinsic factor is essential for absorption of vitamin B12 in the ileum, is secreted by the parietal cells along with the secretion of HCl. When parietal cells of the stomach are destroyed, which frequently occurs in chronic gastritis, the person develops not only achlorhydria (lack of stomach acid secretion) but often also pernicious anemia.

Secretion and Activation of Pepsinogen.

Several slightly different types of pepsinogen are secreted by the peptic and mucous cells of the gastric glands, perform the same functions.

Pepsinogen is activated by HCl to pepsin which functions as an active proteolytic enzyme in a highly acid medium (optimum pH 1.8 to 3.5), but above a pH of about 5 it has almost no proteolytic activity and becomes completely inactivated in a short time.

Regulation of *pepsinogen secretion*

 (1) stimulation of the *peptic cells by acetylcholine* released from the *vagus nerves or from the gastric enteric nervous plexus*
 (2) *stimulation of peptic cell* secretion in response to acid in the stomach. The acid probably does not stimulate the peptic cells directly but instead elicits additional enteric nervous reflexes that support the original nervous signals to the peptic cells

Pyloric Glands—Secretion of Mucus and Gastrin

➢The pyloric glands are structurally similar to the oxyntic glands but contain few peptic cells and almost no parietal cells. Instead, they contain mostly mucous cells that are identical with the mucous neck cells of the oxyntic glands.

➢Secrete small amount of pepsinogen, and an especially large amount of thin mucus

➢Also secrete the hormone gastrin, which plays a key role in controlling gastric secretion.

PYLORIC GLAND
- Surface mucous cell
- NE)
- Mucous neck cell
- G cell (gastrin)
- D cell (somatostatin)

Surface Mucous Cells

➢The entire surface of the stomach mucosa between glands has a continuous layer of a special type of mucous cells called simply "surface mucous cells."

➢They secrete large quantities of viscid alkaline mucus protecting from highly acidic, proteolytic stomach secretion. Contact with food or any irritation of the mucosa directly stimulates them.
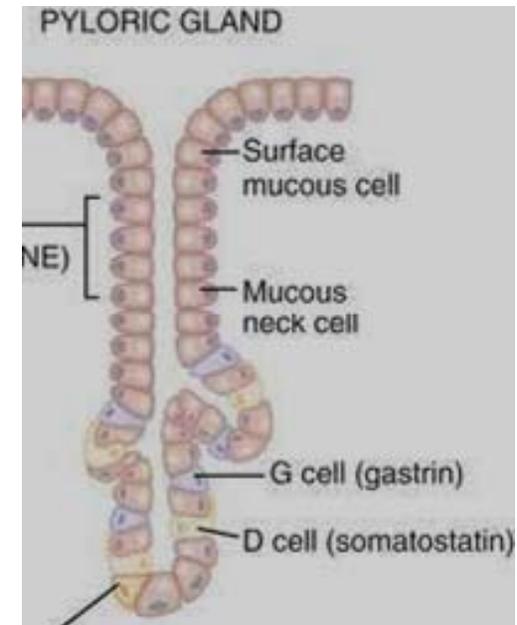
Stimulation of Gastric Acid Secretion

Secretion of acid by Parietal Cells of the Oxyntic glands is under continuous control by both endocrine and nervous signals.

➤Parietal cells operate in close association with another type of cell called enterochromaffin like cells (ECL cells), the primary function of which is to secrete histamine which regulates HCl formation and secretion.

➤ECL cells are stimulated to secrete histamine by the hormonal substance gastrin, which is formed by Pyloric glands in response to proteins in the foods being digested.

➤The ECL cells may also be stimulated by hormonal substances secreted by the enteric nervous system of the stomach wall.

OXYNTIC GLAND

Surface mucous cell —

Parietal cell —

Mucous neck cell —

Enterochromaffin-like cell (histamine) —

D cell (somatostatin) —

Chief cell (pepsinogen) —

Enterochromaffin cell (ANP) —

➤EC cells are neuroendocrine cells. As enteric afferent and efferent nerves do not protrude into the intestinal lumen, EC cells act as a form of sensory transduction to ENS. Secrete serotonin & Atrial natriuretic peptide (ANP) to regulate sensory and motor gastrointestinal reflexes & antral somatostatin secretion resp. by binding to receptors on ENS neurons.
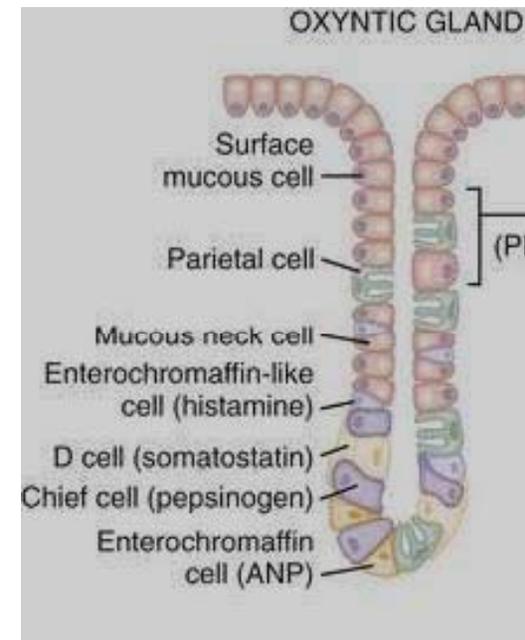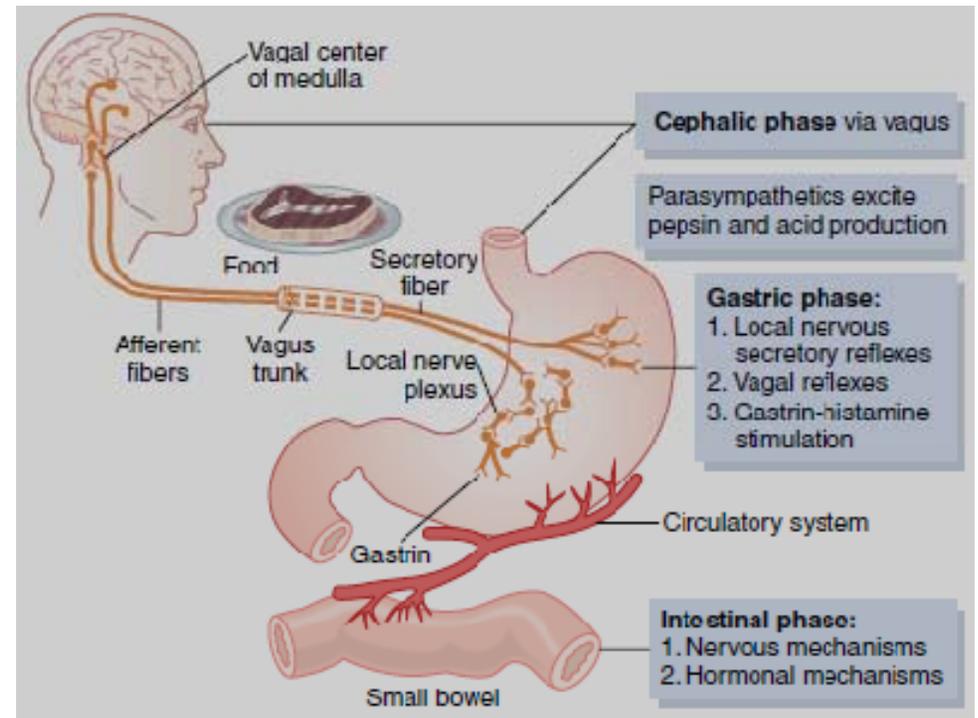
Phases of Gastric Secretion

Cephalic Phase (30%). Occurs even before food enters the stomach, while it is being eaten. It results from the sight, smell, thought, or taste of food, and the appetite. Neurogenic signals originate in the cerebral cortex and in the appetite centers of the amygdala and hypothalamus, transmitted through the dorsal motor nuclei of the vagi and thence through the vagus nerves to the stomach.

(emotional stimuli can cause peptic ulcers by increasing gastric secretion, like the cephalic phase)

Gastric Phase (60%). Once food enters the stomach, it excites (1) long vagovagal reflexes from the stomach to the brain and back to the stomach, (2) local enteric reflexes, and (3) the gastrin mechanism,

Intestinal Phase. (10%) Presence of food in the upper portion of the small intestine, particularly in the duodenum, will continue to cause stomach secretion of small amounts of gastric juice, probably partly because of small amounts of gastrin released by the duodenal mucosa.

Inhibition of Gastric Secretion by Intestinal Factors

Although intestinal chyme slightly stimulates gastric secretion during the early intestinal phase of stomach secretion but inhibits gastric secretion at other times due to :

1. **Neuronal Inhibition:** The presence of food in the small intestine initiates **a** *reverse enterogastric reflex, transmitted through the* myenteric nervous system and extrinsic sympathetic and vagus nerves, that inhibits stomach secretion. (stimulated by distention, acid, protein breakdown products, or by irritation of the mucosa)

2. **Hormonal Inhibition:** The presence of acid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids, or any irritating factor in the upper small intestine causes release of several intestinal hormones. S*ecretin, stimulates* pancreatic secretion & opposes stomach secretion, GIP, VIP and somatostatin *slight to* moderate inhibition.

(These factors also reduce motility, to slow passage of chyme)

Chemical Composition of Gastrointestinal Hormones: *Gastrin, cholecystokinin (CCK), and secretin are all large* polypeptides (2, 4.2 & 3.4 kDa). The terminal 5 aa in the gastrin and CCK molecular chains are the same. The functional activity of gastrin resides in the terminal 4aa, CCK in the terminal 8aa. All the aa in the secretin molecule are essential. A synthetic gastrin (penagastrin) of the terminal 4 aa of natural gastrin plus the amino acid alanine, has all the same physiologic properties as the natural gastrin.

Pancreatic Secretion

Most of its internal structure similar to that of the salivary glands

➤The pancreatic digestive enzymes are secreted by pancreatic acini, and large volumes of sodium bicarbonate solution are secreted by the small ductules and larger ducts leading from the acini
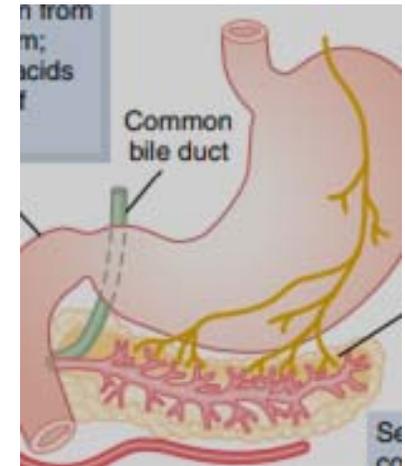
➤The combined product of enzymes and sodium bicarbonate then flows through a long pancreatic duct that normally joins the hepatic duct immediatelybefore it empties into the duodenum through the papilla of Vater, surrounded by the sphincter of Oddi.

➤Pancreatic juice is secreted most abundantly in response to the presence of chyme in the upper portions of the small intestine, and the characteristics of the pancreatic juice are determined to some extent by the types of food in the chyme.

Pancreatic Digestive Enzymes

Protein Digestion: Most important of the pancreatic enzymes for digesting proteins are trypsin, chymotrypsin (digested proteins into peptides), and carboxypolypeptidase (peptides into individual amino acids). By far the most abundant of these is trypsin.

Carbohydrate Digestion: Pancreatic amylase, which hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few trisaccharides.

Fat Digestion: (1) pancreatic lipase, which is capable of hydrolyzing neutral fat into fatty acids and monoglycerides; (2) cholesterol esterase, which causes hydrolysis of cholesterol esters; and (3) phospholipase, which splits fatty acids from phospholipids

Regulation of Enzymatic activity

➢Proteolytic digestive enzymes are in the inactive forms trypsinogen, chymotrypsinogen, and procarboxypolypeptidase, become activated only after they are secreted into the intestinal tract.

➢Trypsinogen is activated by an enzyme called enterokinase, which is secreted by the intestinal mucosa when chyme comes in contact with the mucosa.

➢ Also, trypsinogen can be autocatalytically activated by trypsin that has already been formed from previously secreted trypsinogen. Chymotrypsinogen is activated by trypsin to form chymotrypsin, and procarboxypolypeptidase is activated in a similar manner.

Secretion of Trypsin Inhibitor Prevents Digestion of the Pancreas Itself.

Galndular cells that secrete proteolytic enzymes into the acini of the pancreas also secrete trypsin inhibitor (Pancreatic secretory trypsin inhibitor (PSTI)/ serine protease inhibitor Kazal type I(SPINK1). Trypsin inhibition subsequently inhibits other enzymes as well.

Acute pancreatitis: When pancreas becomes severely damaged or when a duct becomes blocked, accumulation of large quantities of pancreatic secretion, the effect of trypsin inhibitor is often overwhelmed leading to digestion of pancreas with in few hours resulting in circulatory shock or pancreatic insufficiency.

Secretion of Bicarbonate Ions

Pancreatic juice, bicarbonate ions and water, are secreted mainly by the epithelial cells of the ductules and ducts that lead from the acini.

1. HCO3- ions formed by CA enzyme are actively transported in association with Na+ ions through the luminal border of the cell into the lumen of the duct.

2. H+ ions formed by dissociation of carbonic acid inside the cell are exchanged for Na+ ions through the blood border of the cell by a secondary active transport process. This supplies the Na+ that are transported through the luminal border into the pancreatic duct lumen to provide electrical neutrality for the secreted bicarbonate ions.
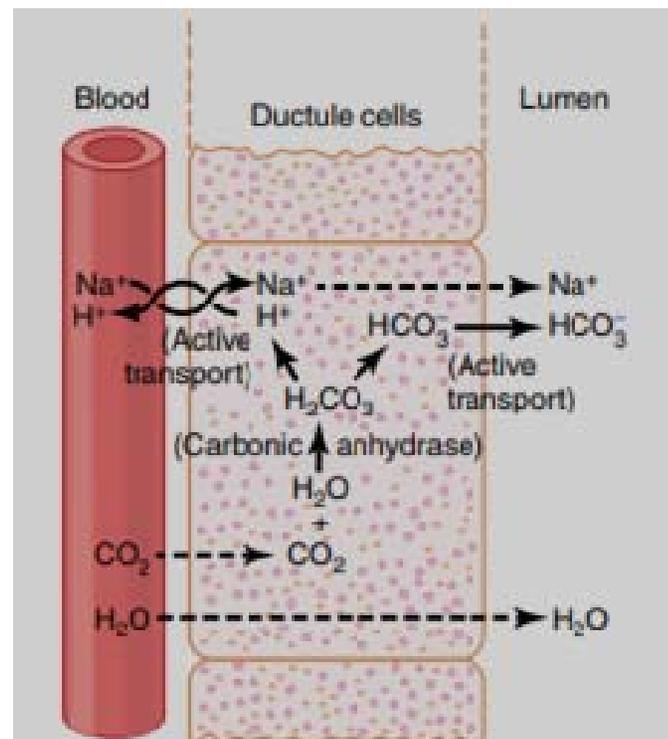
3. The overall movement of Na+ and HCO3- ions from the blood into the duct lumen creates an osmotic pressure gradient that causes osmosis of water also into the pancreatic duct, thus forming an almost completely isosmotic HCO3- solution